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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,402	12/22/2005	Christine Margarete Unger	MXI-352USRCE	6754

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EXAMINER

GUCKER, STEPHEN

ART UNIT	PAPER NUMBER
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1649

MAIL DATE	DELIVERY MODE
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12/22/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,402

Applicant(s)

UNGER ET AL.

Examiner

STEPHEN GUCKER

Art Unit

1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-31 is/are pending in the application.
- 4a) Of the above claim(s) 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23 and 29 is/are rejected.
- 7) ☒ Claim(s) 24-28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-940)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Response to Amendment

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/15/10 has been entered.
2. The previous rejection of record for new matter is withdrawn and a new rejection under 35 USC 112, 1st paragraph is made below. The 35 USC 103 rejection is maintained.
3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 and 29-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes the 6 CDR domains, 3 for the variable light chain (VL) and 3 for the variable heavy chain (HL), for the genus of NP-B antibodies that possess the functional attributes of claim 23: binds to NP-1 and inhibits angiogenesis of a cell expressing NP-1

without inhibiting the binding of VEGF165 to NP-1. However, these grouped sets of CDR triplets could only be determined by trial and error as shown in the instant specification because of the unpredictable and complex interactions between each of the three CDR peptide sequences. As the disclosure notes, often a NPB will inhibit angiogenesis but will also inhibit the binding of VEGF165 to NP-1. It was unexpected to discover a NPB that could bind NP-1, not inhibit the binding of VEGF165 to NP-1, yet still demonstrate anti-angiogenesis function in the assay system. Therefore, the broad genus that is recited in claims 23 and 29 is not commensurate with the written description of the disclosure because the specification cannot adequately describe sufficient members of the genus of claim 23 without be limited to the structural limitations recited in claims 24-28. When a claim recites a functional limitation, especially one the instant disclosure admits is unexpected to find even a single member of a genus that can meet said functional limitation, then such a genus must by necessity be limited to what the specification can envision and describe. Hence, the specification does not adequately describe a sufficient number of the functionally defined broad genus of claims 23 and 29-30 because of the complex and unpredictable nature of protein interactions, particularly when the claims lack any critical core structural limitations.

Vas-cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification should "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116).

The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L.P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying

characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. As such, the teachings of the specification are sufficient to support the breadth of claims 24-28 because an adequate description of the structures that possess the recited functions has been made so that the breadth is commensurate with the disclosure because of the critical core structural limitations recited in the claims. The Revised Interim Guidelines state:

"The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (col. 3, page 71434), "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (col. 2, page 71436).

An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998), *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*, *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021

(Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

Based on the Applicant's specification, the skilled artisan cannot envision the detailed chemical structure corresponding to antibodies that possess the functional properties of claim 23 independent of the structural guidance of the disclosure which supports claims 24-28 because the genus of claims 23 and 29-30 is unduly broad because it encompasses every structure that can perform the recited function regardless if that structure has any similarity with the structures envisioned in the specification.

Thus, for the reasons outlined above, it is concluded that the claims do not meet the requirements for written description under 35 U.S.C. 112, first paragraph. Applicant is

reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Soker et al. ("Soker") in view of Elledge et al. (US 6,218,109 B1; "Elledge").

Soker teaches an antibody that binds to neuropilin-1 (NP-1) but still allows NP-1 and VEGF165 to bind to each other (abstract, Figure 1, and pages 360-362 and 365. See page 358 for anti-NP-1 antibody compositions available from Santa Cruz Biotechnology). Soker does not teach monoclonal antibodies to NP-1. Elledge teaches that monoclonal antibodies can be produced by techniques which are well known (column 32, lines 12-22). It would have been obvious to one of ordinary skill in the art at the time of the invention to make generic monoclonal antibodies that bind NP-1 without inhibiting the binding of VEGF165 to NP-1 because the polyclonal antibodies that were used by Soker were known in the prior art and

possessed the recited functional property of the instant invention. The motivation to make anti-NP-1 monoclonal antibodies is because of the advantages to produce them in large quantities and the homogeneity of the product as suggested by Elledge (column 32, lines 12-22). Finally, the antibodies of Soker do meet the limitation of binding cell surface NP-1 (see pages 364-367 and Figure 6 in particular for example).

Applicant's arguments filed 6/15/10 have been fully considered but they are not persuasive. Applicant argues that the antibody of Soker would not necessarily inhibit angiogenesis as claimed. However, absolute certainty is not the standard by which obviousness rejections are made. Since several species of antibody that bind NP-1 act to inhibit angiogenesis regardless of their "expected" effect on the binding of VEGF165 to NP-1, it would seem that the antibody of Soker has a reasonable expectation of also inhibiting angiogenesis because it binds NP-1.

5. Claims 24-28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Gucker

December 21, 2010

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649